WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding a polypeptide
comprising at least one of the biological activities of
Osteoprotegerin wherein the nucleic acid is selected
from the group consisting of:

    a) the nucleic acids shown in Figures 2B (SEQ
ID NO: 2), 9A (SEQ ID NO: 4), and 9B (SEQ ID NO:
6) or complementary strands thereof;

    b) nucleic acids which hybridize under
stringent conditions with the polypeptide-encoding
regions as shown in Figures 2B (SEQ ID NO: 1), 9A (SEQ
ID NO: 3) and 9B (SEQ ID NO: 5);

    c) nucleic acids which hybridize under
stringent conditions with nucleotides 148 through 337
inclusive as shown in Figure 2B; and

    d) nucleic acid which are degenerate to the
nucleic acids of (a), (b) and (c).

2. The nucleic acid of Claim 1 which is cDNA,
genomic DNA, synthetic DNA or RNA.

3. A polypeptide encoded by the nucleic acid of
Claim 1.

4. The nucleic acid of Claim 1 including one or
more codons preferred for Escherichia coli expression.

5. The nucleic acid of Claim 1 having a detectable
label attached thereto.

6. The nucleic acid of Claim 1 comprising the
polypeptide-encoding region of Figure 2B (SEQ ID NO:
1), Figure 9A (SEQ ID NO: 3) or Figure 9B (SEQ ID
NO: 5).

7. The nucleic acid of Claim 6 having the sequence as shown in Figure 9B from nucleotides 158-1297.

5   8. An expression vector comprising the nucleic acid of Claim 1.

9. The expression vector of Claim 8 wherein the nucleic acid comprises the polypeptide - encoding region
10   as shown in Figure 9B (SEQ ID NO: 5).

10. A host cell transformed or transfected with the expression vector of Claim 8.

15   11. The host cell of Claim 10 which is a eucaryotic cell.

12. The host cell of Claim 11 which is selected from the group consisting of CHO, COS, 293, 3T3, CV-1
20   and BHK cells.

13. The host cell of Claim 10 which is a procaryotic cell.

25   14. The host cell of Claim 13 which is *Escherichia coli*.

15. A transgenic mammal comprising the expression vector of Claim 8.

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16. The transgenic mammal of Claim 15 which is a rodent.

17. The transgenic mammal of Claim 16 which is a
35   mouse.

18. A process for the production of Osteoprotegerin comprising:

    growing under suitable nutrient conditions host cells transformed or transfected with the nucleic
5   acid of Claim 1; and

    isolating the polypeptide products of the expression of the nucleic acids.

    19. A purifed and isolated polypeptide comprising
10 Osteoprotegerin.

    20. The polypeptide of Claim 19 which is mammalian Osteoprotegerin.

15   21. The polypeptide of Claim 20 which is human Osteoprotegerin.

    22. The polypeptide of Claim 19 which is substantially free of other human proteins.
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    23. The polypeptide of Claim 21 having the amino acid sequence as shown in Figure 2B (SEQ ID NO: 2), Figure 9A (SEQ ID NO: 4), or Figure 9B (SEQ ID NO: 6) or a derivative thereof.
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    24. The polypeptide of Claim 23 having the amino acid sequence as shown in Figure 9B from residues 22-401 inclusive.

30   25. The polypeptide of Claim 23 having the amino acid sequence as shown in Figure 9B (SEQ ID NO: 6) from residues 32-401 inclusive.

    26. The polypeptide of Claim 19 which is
35 characterized by being a product of expression of an exogenous DNA sequence.

27. The polypeptide of Claim 26 wherein the DNA is cDNA, genomic DNA or synthetic DNA.

28. The polypeptide of Claim 19 which has been modified with a water-soluble polymer.

29. The polypeptide of Claim 28 wherein the water soluble polymer is polyethylene glycol.

30. An antibody or fragment thereof which specifically binds to Osteoprotegerin.

31. The antibody of Claim 30 which is a monoclonal antibody.

32. A method for detecting the presence of Osteoprotegerin in a biological sample comprising:
        incubating the sample with the antibody of Claim 30 under conditions that allow binding of the antibody to osteoprotegerin; and
        detecting the bound antibody.

33. A method to assess the ability of a candidate substance to bind to Osteoprotegerin comprising:
        incubating Osteoprotegerin with the candidate substance under conditions that allow binding; and
        measuring the bound substance.

34. A method of regulating the levels of osteoprotegerin in an animal comprising modifying the animal with a nucleic acid encoding Osteoprotegerin.

35. The method of Claim 34 wherein the nucleic acid promotes an increase in the tissue level of Osteoprotegerin.

36. The method of Claim 35 wherein the animal is a human.

5   37. A pharmaceutical composition comprising a therapeutically effective amount of osteoprotegerin in a pharmacetically acceptable carrier, adjuvant, solubilizer, stabilizer and/or anti-oxidant.

10   38. The composition of Claim 37 wherein the Osteoprotegerin is human Osteoprotegerin.

39. The composition of Claim 38 wherein the Osteoprotegerin has the amino acid sequence as shown in
15   Figure 9B.

40. A method of treating a bone disorder comprising administering a therapeutically effective amount of the polypeptide of Claim 19.

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41. The method of Claim 40 wherein the polypeptide is human Osteoprotegerin.

42. The method of Claim 40 wherein the bone
25   disorder is excessive bone loss.

43. The method of Claim 42. wherein the bone disorder is selected from the group consisting of osteoporosis, Paget's disease of bone, hypercalcemia,
30   hyperparathyroidism, steroid-induced osteopenia, bone loss due to rheumatoid arthritis, bone loss due to osteomyelitis, osteolytic metastasis, and peridonatal bone loss.

35   44. The method of Claim 38 further comprising administering a therapeutically effective amount of a

substances selected from the group consisting of bone
morphogenic proteins BMP-1 through BMP-12, TGF-β family
members, IL-1 inhibitors, TNFα inhibitors, parathyroid
hormone and analogs thereof, parathyroid hormone related
5   protein and analogs thereof, E series prostaglandins,
bisphosphonates, and bone-enhancing minerals.